

WHAT IS CLAIMED IS:

- Subst
AI
- 004477-56260
1. A system for detecting an analyte having a mass, the system comprising:
a light source;
a structure having an immobilized portion and a second portion adapted for resonating, wherein said second portion is illuminated by said light source, further wherein said structure has an immobilized binding partner that binds to said analyte on said second portion of the structure, wherein said structure resonates under ambient conditions at a frequency based on the mass of said analyte on said second portion; and
a photodetector responsive to light reflected by said structure, wherein said photodetector provides an output corresponding to a resonant frequency of said structure.
 2. The system of claim 1 further comprising a processor coupled to said photodetector for determining the mass of said analyte.
 3. The system of claim 1 further comprising a spectrum analyzer coupled to said photodetector for determining a resonant frequency of said structure.
 4. The system of claim 1 where said photodetector comprises a split photodiode.
 5. The system of claim 1 where said photodetector comprises a first photodiode and a second photodiode.
 6. The system of claim 1 wherein said photodetector is adapted for generating a differential voltage signal.
 7. The system of claim 1 wherein said binding partner is immobilized near said second end of said structure.

8. The system of claim 1 wherein said structure comprises silicon, silicon nitride, silicon dioxide, silicon carbide, polysilicon, carbon, diamond-like carbon film, metal or gallium arsenide.
9. The system of claim 1 wherein said immobilized portion is rigidly coupled to a support.
10. The system of claim 1 wherein said structure is adapted for vibrating under ambient conditions including thermal noise.
11. The system of claim 1 wherein said structure is adapted for vibrating under ambient conditions including ambient air vibrations.
12. The system of claim 1 wherein said structure is coupled to a piezoelectric drive.
13. The system of claim 1 further comprising a vacuum environment in which said structure operates.
14. The system of claim 1 wherein the analyte is a pathogen.
15. The system of claim 1 wherein the analyte is a microorganism.
16. The system of claim 1 wherein the analyte is a bacteria, a virus or a subunit thereof.
17. The system of claim 1 wherein the binding partner for the analyte is an antibody that binds to said analyte.
18. The system of claim 1 wherein the binding partner is a cellular receptor that binds to a ligand.

19. The system of claim 1 wherein the analyte is a ligand specific for a cellular receptor.
20. The system of claim 1 wherein the analyte is a metallic ion and the binding partner is a chelator that binds said metallic ion.
21. The system of claim 1 wherein the binding partner includes a DNA sequence and the analyte includes a complementary DNA sequence.
22. The system of claim 1 wherein said structure comprises a cantilever beam.
23. The system of claim 22 wherein said cantilever beam vibrates in an out of plane mode.
24. The system of claim 22 wherein said cantilever beam has a length of 0.5 to 1000 μm .
25. The system of claim 1 wherein said structure comprises a linear member having a first end, a second end, and a middle region, and wherein said immobilized portion includes said first end and said second end, and wherein said second portion includes said middle region.
26. The system of claim 1 wherein said structure comprises a disk-shaped member having a perimeter and a center region, and wherein said immobilized portion includes said perimeter, and wherein said second portion includes said center region.
27. A method for detecting a pathogen comprising:
providing a cantilever beam having an immobilized binding partner for said pathogen on a surface of said cantilever beam, said cantilever beam adapted for oscillating relative to a stationary substrate;

optically determining a first resonant frequency for said beam when said beam is excited by ambient conditions;

exposing said cantilever beam to a liquid mixture suspected of containing said pathogen;

optically determining a second resonant frequency for said beam when said beam is excited by ambient conditions after said beam is exposed to said liquid mixture; and

determining a mass difference for said beam based on a difference between said first resonant frequency and said second resonant frequency.

28. The method of claim 27 wherein optically determining a first resonant frequency and optically determining a second resonant frequency comprises:

illuminating said beam using a laser light source; and

sensing light reflected by said beam using a photodetector.

29. The method of claim 28 wherein sensing light reflected by said beam using a photodetector comprises generating a differential voltage signal.

30. The method of claim 28 wherein sensing light reflected by said beam using a photodetector comprises sensing a first reflected light from said surface of said cantilever beam and sensing a second reflected light from said substrate.

31. The method of claim 29 wherein said photodetector is sensitive to interference between said first reflected light and said second reflected light.

32. The method of claim 29 further comprising an external drive adapted for oscillating said cantilever beam at a predetermined frequency.

33. The method of claim 27 wherein ambient conditions include thermal mechanical noise and ambient air vibrations.

34. The method of claim 27 wherein immobilizing a binding partner for said pathogen on a surface of said cantilever beam comprises:
 - contacting said beam in a first liquid mixture comprising said binding partner for said pathogen;
 - removing unbound components of the liquid from said beam; and
 - drying said beam in an inert atmosphere.
35. The method of claim 27 wherein removing unbound components of the liquid from said beam comprises rinsing said beam.
36. The method of claim 27 wherein removing unbound components of the liquid from said beam comprises ~~rinsing~~ said beam with water.
37. The method of claim 27 wherein exposing said cantilever beam to a mixture suspected of containing said pathogen comprises:
 - immersing said beam in a liquid mixture suspected of containing said pathogen so that said binding partner binds to said pathogen;
 - incubating said beam for a predetermined period of time;
 - removing unbound components of the liquid from said beam; and
 - drying said beam in an inert atmosphere.
38. The method of claim 27 wherein exposing said cantilever beam to a mixture comprises exposing said cantilever beam to a buffered aqueous solution.
39. The method of claim 27 wherein said pathogen includes a microorganism.
40. The method of claim 27 further comprising preparing a second beam and immersing said second beam in a second liquid mixture suspected of containing a second pathogen.

41. The method of claim 27 further comprising providing a vacuum environment for said cantilever beam.
42. The method of claim 27 wherein mechanical properties of said beam are tailored to detect a mass difference in the range of 10^{-8} to 10^{-18} grams.
43. The method of claim 27 wherein mechanical properties of said beam are tailored to achieve a desired resonant frequency.
44. An array of analyte detectors comprising:
a plurality of cantilever beams, each of said beams having a mass, a first end and a second end, wherein said first end is immobilized and wherein each of said beams resonates in an out of plane mode under ambient conditions at a frequency based on said mass of said cantilever beam;
a plurality of immobilized binding partners on a surface of said second end of each of said plurality of cantilever beams, wherein each of said immobilized binding partners binds to a predetermined analyte; and
a sensor responsive to light reflected by a particular beam selected from said plurality of cantilever beams, wherein said sensor generates an output signal based on a resonant frequency of said particular beam.
45. The array of claim 44 wherein said plurality of cantilever beams comprises silicon nitride.
46. The array of claim 44 further comprising a light source illuminating said particular beam.
47. The array of claim 44 wherein said plurality of immobilized binding partners are heterogeneous.

48. The array of claim 44 wherein said plurality of immobilized binding partners are homogenous.

49. A detector for an analyte comprising:
binding means for binding with said analyte;
cantilever means for resonating under ambient conditions, wherein the binding means is immobilized on a portion of said cantilever means and wherein the cantilever means resonates in a first mode at a first resonant frequency;
sensor means for determining said first resonant frequency; and
processor means for determining a mass of analyte based on a difference between said first resonant frequency and a second resonant frequency after exposure of said binding means to said analyte.

50. The detector of claim 49 wherein said first mode comprises an out of plane mode.

51. The detector of claim 49 wherein said cantilever means comprises silicon, silicon nitride, silicon dioxide, silicon carbide, polysilicon, carbon, diamond-like carbon film, metal or gallium arsenide.

52. The detector of claim 49 wherein said sensor means comprises a photodiode.

53. The detector of claim 49 wherein said processor means comprises a frequency analyzer.

54. The detector of claim 49 wherein said binding means is immobilized at a location proximate to an unsupported end of said cantilever means.

55. The detector of claim 49 wherein said cantilever means is aligned substantially horizontally.

56. The detector of claim 49 further comprising a vacuum encapsulating said cantilever means.

57. A system for detecting an analyte having a mass, the system comprising:

a light source;

a cantilever beam having a first end and a second end, wherein said first end is immobilized and said second end is illuminated by said light source, further wherein said cantilever beam has an immobilized binding partner that binds to said analyte on a surface of the beam;

a beam driver in communication with said cantilever beam, said driver for vibrating said cantilever beam at a predetermined frequency, wherein the amplitude of vibrations of said cantilever beam are based on the mass of said analyte on said cantilever beam; and

a photodiode responsive to light reflected by said cantilever beam, wherein said photodiode provides an output corresponding to said vibration frequency and vibration amplitude of said cantilever beam.

58. The system of claim 57 wherein said beam driver is adapted for vibrating said cantilever beam at a plurality of particular frequencies.

59. A system for detecting an analyte having a mass, the system comprising:

a light source adapted for projecting a ray of light;

a cantilever beam having a free end and a stationary end, said stationary end affixed to a substrate and said free end adapted for vibrating on a transverse axis at a predetermined frequency, said transverse axis being relative to said cantilever beam, said substrate having a portion substantially parallel with, and located beneath, said cantilever beam, said cantilever beam having a thickness that is partially transparent to said ray of light;

a driver coupled to said substrate and adapted for vibrating said cantilever beam on said transverse axis; and

a photodetector adapted for receiving light reflected by said cantilever beam and light reflected by said substrate.

60. The system of claim 59 further comprising a beam splitter adapted for passing light incident to said cantilever beam and reflecting light reflected by said cantilever beam and light reflected by said substrate.

61. The system of ~~claim 59~~ further comprising a spectrum analyzer adapted for receiving a signal generated by said photodetector.

004477 55/260